Abstract

An aromatic ring chosen from a derivative of toluene or a condensed polycyclic aromatic hydrocarbon is an allosteric inhibitor of the retroviral Tat protein. Interaction of these inhibitors with the Tat protein prevents the conformational changes associated with transactivation activity. These derivatives advantageously avoid pitfalls associated with previous competitive inhibitors and allow inhibition of both intracellular and extracellular Tat activity. The invention provides methods of making the inhibitors, as well as medicaments and pharmaceutical compositions comprising the inhibitors, which are useful in treating retroviral diseases associated with Tat activity, such as HIV.